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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/698,213	10/30/2000	James D. McIninch	04983.0220.00US00/38-10(1	6072
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ARNOLD & PORTER IP DOCKETING DEPARTMENT; RM 1126(b) 555 12TH STREET, N.W. WASHINGTON, DC 20004-1206			ART UNIT 1631	PAPER NUMBER

DATE MAILED: 12/15/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

09/698,213

Applicant(s)

MCININCH, JAMES D.

Examiner

Carolyn L Smith

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 12 August 2003 and 14 August 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 1-16 and 41-44 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-16 and 41-44 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

## Priority under 35 U.S.C. §§ 119 and 120

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 13) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.
- a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

## Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 08142003. 6) ☐ Other: \_\_\_\_\_

### **DETAILED ACTION**

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicants' submissions, filed 08/12/03 and 08/14/03, have been entered. Amended claims 1-4, 6-11, 13, 16, and 41-44 are acknowledged.

Claims herein under examination are 1-16 and 41-44.

### ***Claim Rejections - 35 USC § 101***

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-16 and 41-42 are rejected under 35 U.S.C. 101 because the claims are directed to non-statutory subject matter. Read in light of the specification, claims 1-16 and 41-42 encompass methods that can be performed on a computer. As written, these claims appear to lack any physical result performed outside of a computer.

As stated in MPEP § 2106, (IV)(2)(b), to be statutory, a claimed computer-related process must either: (A) result in a physical transformation outside the computer for which a practical application in the technological arts is either disclosed in the specification or would

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have been known to a skilled artisan (discussed in MPEP § 2106 (IV)(2)(b)(i)), or (B) be limited to a practical application within the technological arts (discussed in MPEP § 2106 (IV)(2)(b)(ii)).

As stated in MPEP § 2106 (IV)(2)(b)(i), the independent physical acts may be post- or pre-computer processing activity as described below:

A process is statutory if it requires physical acts to be performed outside the computer independent of and following the steps to be performed by a programmed computer, where those acts involve the manipulation of tangible physical objects and result in the object having a different physical attribute or structure. *Diamond v. Diehr*, 450 U.S. at 187, 209 USPQ at 8. Thus, if a process claim includes one or more post-computer process steps that result in a physical transformation outside the computer (beyond merely conveying the direct result of the computer operation), the claim is clearly statutory.

Another statutory process is one that requires the measurements of physical objects or activities to be transformed outside of the computer into computer data (In re Gelnovatch, 595 F.2d 32, 41 n.7, 201 USPQ 136, 145 n.7 (CCPA 1979) (data-gathering step did not measure physical phenomenon); *Arrhythmia*, 958 F.2d at 1056, 22 USPQ2d at 1036), where the data comprises signals corresponding to physical objects or activities external to the computer system, and where the process causes a physical transformation of the signals which are intangible representations of the physical objects or activities. *Schrader*, 22 F.3d at 294, 30 USPQ2d at 1459 citing with approval *Arrhythmia*, 958 F.2d at 1058-59, 22 USPQ2d at 1037-38; *Abele*, 684 F.2d at 909, 214 USPQ at 688; In re *Taner*, 681 F.2d 787, 790, 214 USPQ 678, 681 (CCPA 1982).

As stated in MPEP § 2106 (IV)(2)(b)(ii), the computer-related process may be limited to a practical application in the technological arts as described below:

There is always some form of physical transformation within a computer because a computer acts on signals and transforms them during its operation and changes the state of its components during the execution of a process. Even though such a physical transformation occurs within a computer, such activity is not determinative of whether the process is statutory because such transformation alone does not distinguish a statutory computer process from a nonstatutory computer process. What is determinative is not how the computer performs the process, but what the computer does to achieve a practical application. See *Arrhythmia*, 958 F.2d at 1057, 22 USPQ2d at 1036.

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Claims 1-16 and 41-42 do not fulfill either of these statutory requirements and are therefore rejected under 35 U.S.C. 101 because the claims are directed to non-statutory subject matter.

Claims 1-16 and 41-42 are rejected under 35 U.S.C. 101 because the claims are directed to non-statutory subject matter. As written, the claims appear to be directed to methods that merely manipulates numbers, abstract concepts or ideas, or signals representing any of the foregoing.

As stated in MPEP § 2106, (IV)(B)(1), If the “acts” of a claimed process manipulate only numbers, abstract concepts or ideas, or signals representing any of the foregoing, the acts are not being applied to appropriate subject matter. *Schrader*, 22 F.3d at 294-95, 30 USPQ2d at 1458-59. Thus, a process consisting solely of mathematical operations, i.e., converting one set of numbers into another set of numbers, does not manipulate appropriate subject matter and thus cannot constitute a statutory process.

In practical terms, claims define nonstatutory processes if they:

- consist solely of mathematical operations without some claimed practical application (i.e., executing a “mathematical algorithm”); or
- simply manipulate abstract ideas, e.g., a bid (*Schrader*, 22 F.3d at 293-94, 30 USPQ2d at 1458-59) or a bubble hierarchy (*Warmerdam*, 33 F.3d at 1360, 31 USPQ2d at 1759), without some claimed practical application.

Claims 1-16 and 41-42 do not fulfill any of these statutory requirements and are therefore rejected under 35 U.S.C. 101 because the claims are directed to non-statutory subject matter.

***Claims Rejected Under 35 USC § 112, First Paragraph***

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

**LACK OF WRITTEN DESCRIPTION**

Claims 1-16 and 41-44 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time of the invention was filed, had possession of the claimed invention.

Applicant states that written support for the amendments to the claims can be found in the specification on pages 17 (lines 17-20), 18 (lines 11-15), 21 (line 1) through 26 (line 26), 46 (line 1) through 48 (line 10), and Example 2.

Claims 1-4, 6-11, 13, 16, and 41-44 have been amended to include the term “selected” which is not supported in the passages of the specification listed above. The specification states a single nucleotide, such as on page 21, line 8, but it makes no mention of whether this nucleotide was selected or randomly chosen.

Claims 1 (lines 14-15), 7 (lines 14-15), 8 (lines 13-14), 43 (lines 16-17), and 44 (lines 14-16) recite the phrase “wherein said bias function does not have the same value in all of said states for said selected nucleotide” which is not supported in the passages of the specification listed above. The scope of the claims is broader than the support found in the specification. For example, as stated on page 21, lines 1-6, bias can be the value of one for at least one state and a value other than one for at least one state. However, this does not provide written support that

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the bias function does not have the same value in all of said states, which can be reasonably interpreted to mean all values must be different.

Claims 6 and 16 recite the phrase bias “function has a value’ between 0.0 and 0.9, or greater than 1.1”. It is unclear what the term “value” is intended to mean. If value is intended to mean “bias” then there is proper written support for this phrase on pages 18 (line 17) and 21 (line 6). However, if the term “value” is intended to mean the resultant value of the bias function, then there is no adequate written support for this term. Because proper claim examination involves using the broadest reasonable interpretation of the claims, the latter definition of “value” is encompassed in claims 6 and 16 which therefore makes the phrase “function has a value” a NEW MATTER issue.

Because the introduction of “selected”, “wherein said bias function does not have the same value in all of said states for said selected nucleotide”, and “function has a value” lacks written basis for amended claims 1-4, 6-11, 13, 16, and 41-44, as filed on 8/14/2003, they are considered NEW MATTER. Claims 5, 12, and 14-15 are also rejected due to their dependency from claims 1 and 8.

### ***Claim Rejections – 35 U.S.C. 112, First Paragraph***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in *Ex parte Forman*, 230 USPQ 546 (BPAI 1986) and

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reiterated by the Court of Appeals in *In re Wands*, 8 USPQ2d 1400 at 1404 (CAFC 1988). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. The Board also stated that although the level of the skill in molecular biology is high, the results of experiments in genetic engineering are unpredictable. While all of these factors are considered, a sufficient amount for a *prima facie* case are discussed below.

#### LACK OF ENABLEMENT

Claims 1-16 and 41-44 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the claimed invention.

Claims 1-16 and 41-44 are rejected because the specification, while being enabling for the following:

Initial oligonucleotide probability	p. 21, equation I,
Transition probability	p. 22, equation II,
Nucleic acid sequence probability	p. 23, equation III, and
Probability for each nucleotide state	p. 24, equation IV,

the specification does not reasonably provide enablement for any method of computation for determining the above probabilities. The specification does not enable any person skilled in the



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art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The instant application fails to provide guidance to one of ordinary skill in the art for generating the probability values of the following by any other means than by the four equations indicated above. The specification does not provide or suggest what any other substitutable methods of computation could be for the above probability determinations thus not enabling one of ordinary skill in the art to know what calculations to perform. While the specification provides some guidance for a method of determining a probability value for the above listing using the particular equations or values disclosed, the specification does not provide guidance for a method of determining the probability by any other means. The specification does not provide working examples of the methods described using any other means of computing the described probability values. While working examples are not, per se, required, the specification must provide adequate guidance such that one of skill in the art could practice the invention without undue experimentation. Given the lack of descriptive working examples in the specification, and the unpredictability of generating probability values, the specification as filed is not enabling for any method of determining the listed probability values as claimed. The instant application is only enabled for the above-mentioned computational means of the four probabilities.

Applicant argues that disclosure of a single species provides sufficient enabling support if one of skill in the art can, using the state of the art and Applicant's written disclosures, practice the invention in its full scope without undue experimentation (RCE Response, filed 08/14/03, page 9, lines 3-5). Applicant argues that a single embodiment may provide broad enablement in cases involving predictable factors (RCE Response, page 9, lines 13-14). These arguments are

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found unpersuasive as the single species concept referring to *In re Wands* appears to be taken out of context. In that court decision, enablement was provided not by just one species, but rather by more than one species in order to provide enablement. The remaining case law noted by applicant is not being addressed due to its appearing to lack correspondence or proper relevance to the issues at hand. The instant invention involves generating probability values which is not considered to include predictable factors. Applicant's request for legal or other support for this issue is denied as sufficient reasoning for the unpredictability conclusion was presented in the previous Office action and applicant has failed to provide sound evidence that this reasoning is improper. Therefore, additional support at this time is not considered to be necessary. Applicant states it is well established law that patent applications are not required to disclose every species enabled by their claims (RCE Response, page 9, lines 16-17). This is found unpersuasive as not every species is required, but rather at least representative species outlining a broad scope of computational practices considered essential matter must be disclosed. As stated in the FINAL action (page 4, lines 10-12), mailed 5/2/03, one of skill in the art would know how to use the method steps with the four above-mentioned enabled probability equations, but not with undisclosed equations. Applicant argues an applicant need only show that one skilled in the art would be able to make and use the claimed invention using the application as a guide (RCE Response, page 9, lines 19-20) and need not disclose what is well-known to those skilled in the art and preferably omits that which is well known to those skilled and already available to the public (RCE Response, page 10, lines 1-3). This is found unpersuasive as the Applicant has not shown that the undisclosed probability equations are, in fact, well known. Applicant submits that the Office failed to provide any evidence to suggest that the statistical methods taught by

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Durbin are not well known in the art. This is found unpersuasive as the previous Office action provided sound reasoning as to why enablement was lacking, including information about a single reference not being considered adequate to support the idea of being well known.

Applicant has failed to provide valid evidence that would suggest that the reasoning provided in the previous Office action is improper. Therefore, a request for additional support, including an affidavit, is not considered to be necessary at this time. Applicant states (RCE Response, page 10, lines 18-21) that any probability model applicable to nucleic acid sequence state probabilities can be used for the probability steps if the output supports the method, including inhomogeneous Markov models having fewer than eight states. This is found unpersuasive as this clearly illustrates that not all probability models support the instant methods. Meanwhile the claims, as written, broadly encompass methods of computation for other probability determinations, besides those equations listed above. Applicants disagree that the Durbin reference is essential material (RCE Response, page 11, lines 3-7). This is found unpersuasive as representative species of undisclosed probability equations which are needed to be included in order to support a broad and generic practice as stated in the instant claims are considered essential material of the claimed invention. As stated in the FINAL rejection (page 4, line 19 to page 5, line 2), mailed 5/2/03, the incorporation of essential material in the specification by reference to a foreign application or patent, or to a publication is improper. It is noted that applicant's reliance on prior art methods may only extend to well known methods and that single specific publications do not support their content as being well known.

***Claims Rejected Under 35 U.S.C. § 112, Second Paragraph***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

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The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 3, 4, 6, 7, 11, 13, 16, and 41-42 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the applicant regards as the invention.

Claims 3 and 11 are vague and indefinite, because they fail to end in a period, thus failing to clarify the end of intended limitation(s) in these claims.

Claims 3 and 11, as currently written, each contain a mathematical equation which is confusing, because the equation incorporates " $\Phi(f)$ " representing bias function which effectively cancels itself out in the equation, and therefore nullifies its effect on the equation. Applicant states " $\Phi(f)$ " does not cancel itself out of the equation, because it corresponds to a function which can have different numerical values corresponding to different elements in the set of states. This is found unpersuasive as the claim can be broadly and reasonably interpreted to contain the same " $\Phi(f)$ " value in the numerator and denominator of the equation since the claim does not suggest otherwise. Applicant is reminded that if the intention is for " $\Phi(f)$ " not to be represented by the same exact number in the numerator and denominator, then subscripts, or some other form of notation, would need to be added to clarify this issue.

Claims 3 and 11 are vague and indefinite due to the lack of clarity in the following terms:  $f$ ,  $S$ ,  $P_f$ ,  $P_i$ , and  $\Phi$ . It is unclear as to what are the metes and bounds of these terms. Applicant states that claim language must be analyzed in light of the application, the prior art teachings, and the claim interpretation from one of ordinary skill in the art. This is found unpersuasive as it is still unclear as to whether Applicant intends to use definitions from the art or those in the

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specification. A listing of the exact definitions of these terms in claims 3 and 11 would clarify this issue. Applicant states that no legal requirement to list “the exact definition of each term” within the claim is known or has been provided. This is found nonpersuasive as adequate reasoning was set forth in the previous Office action, and above, as to why this rejection has been made. Applicant has failed to provide evidence to support this reasoning to be improper. Therefore, additional support at this time is not considered to be necessary.

Claim 4 recites the term “middle nucleotide in said nucleic acid sequence” which is vague and indefinite. It is unclear what would be considered a middle nucleotide if said nucleic acid is made up of  $n$  number of nucleotides where  $n$  is an even integer. Clarification of a “middle nucleotide” in this situation is requested.

Claims 6 and 16 (lines 1-2 of each) recite the phrase “bias function has a value between 0.0 and 0.9, or greater than 1.1” which is vague and indefinite. It is unclear if the “value” is intended to mean the resultant value of the bias function or if it is intended to mean the bias which is a value used in the bias function (as stated on page 18, line 17, of the specification). Clarification of the phrase, particular the intended meaning of “value” is requested via clearer claim wording.

Claim 7, line 14, recites the phrase “accepts a bias function” which is vague and indefinite. It is unclear if the determination step, the probability, or each step is accepting the bias function. Clarification of the metes and bounds of this phrase via clearer claim wording is requested.

Claim 13, line 2, recites the phrase “middle nucleotide in its own window” which is vague and indefinite. It is unclear what would be considered a middle nucleotide if said window

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contains  $n$  number of nucleotides where  $n$  is an even integer. Clarification of a “middle nucleotide” in this situation is requested.

Claim 41, line 4, recites the phrase “a probability of said nucleic acid sequence” which is vague and indefinite. The claim is directed to determining a probability for one or more states for a nucleotide by determining a probability for each state of said nucleotide. Therefore, it is unclear to which probability the probability of line 4 is referring, since several probabilities are stated previously in the claim as well various types of probabilities are stated in the specification. This same issue applies to the probability stated on line 4 of claim 42. Clarification of the metes and bounds of this phrase via clearer claim wording is requested.

### ***Claim Rejections – 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1, 4, 5, 7, 8, 9, 12, 13, 15, and 41-44 are rejected under 35 U.S.C. 103(a) as being obvious over Borodovsky et al. (Computers Chemistry, Volume 17, No. 2, pages 123-133) in view of Selifonov et al. (US 2002/0183934 A1).

Borodovsky et al. describe a computer-implemented method (GENMARK) for determining different state probabilities of a nucleotide in a nucleic acid sequence using non-homogeneous Markov models, including initial and transitional probabilities (abstract and page

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128, col. 1) as stated in claims 1, 7, 8, and 41-44. Borodovsky et al. analyze a nucleotide fragment "F" (page 129, col. 2, paragraph 3) of the nucleic acid sequence of interest, as stated in claims 5 and 12. Borodovsky et al describe using Markov chain models of coding and non-coding regions with a moving window of 96 basepairs with consequent steps moving 6 basepairs (page 125, col. 2, 3<sup>rd</sup> full paragraph). Borodovsky et al. describe probability values calculated for every nucleotide fragment F found in the window opening (window probabilities as well as nucleic acid sequence probabilities) which is reasonably interpreted to be repeating steps a) through d) of claims 8 and 44 for remaining nucleotides. Borodovsky et al. refer to the fragment's middle point (page 129, col. 2, paragraph 1), as stated in claims 4 and 13. Borodovsky et al. describe varying window sizes of 48 to 94 nucleotides in length (page 129, col. 1, last line) which is reasonably interpreted to be a window "of about 75 to 125 nucleotides" in length, as stated in claim 15. The GENMARK method is a program (page 132, col. 2, 2<sup>nd</sup> full paragraph) which is reasonably interpreted to be a program storage device readable by machine, as stated in claims 43 and 44. Borodovsky et al. describe generating a model DNA sequence moving left to right or right to left to define the probability of a nucleotide string (page 128, col. 1, paragraphs 2-3) which is reasonably interpreted to be a determination of nucleic acid sequence probabilities as well as performing step e) of claim 8 sequentially on contiguous nucleotides, as stated in claim 9. However, Borodovsky et al. do not specifically state the application of a bias function to nucleic acid sequence probabilities wherein the bias function does not have the same value in all states for a selected nucleotide.

Selifonov et al. describe methods of generating a diverse population of character strings relating to a biological polymer wherein in these strings are generated by altering pre-existing

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character strings (page 2, paragraph 0014). Selifonov et al. describe the synthesized character strings are selected for one or more activity and a bias may be applied by filtering to display polymers above a desired threshold (page 2, paragraph 0015). Selifonov et al. describe biasing a selected group of strings (page 6, paragraph 0075). Selifonov et al. describe using a bias which imposes discriminating criteria for use of any genetic operators, and various types of positive and negative biases, such as sequence specific features (page 6, paragraph 0080).

Borodovsky et al. state the problem of predicting gene locations in newly sequenced DNA is well known but not resolved (abstract). Borodovsky et al. state large-scale DNA sequencing calls for fast and efficient gene recognition methods to find new genes (page 123, col. 1, lines 1-4). Borodovsky et al. state further improvements of the Markov chain/Bayes method for searching for genes (page 123, col. 2, lines 3-6). Selifonov et al. state rapid evolution of nucleic acids provides for the generation of encoded molecules with new and/or improved properties of industrial, agricultural, and therapeutic importance (page 1, paragraph 0008). Selifonov et al. provide new “in silico” methods modeled in a computer system for guided gene synthesis to avoid physical manipulation of nucleic acids including alterations in pre-existing character strings (page 2, paragraphs 0013 and 0015). It would have been obvious to a person of ordinary skill in the art at the time the invention was made to make further improvements in gene searching programs, as stated by Borodovsky et al., by adding filtering techniques to in order to make searches more efficient. Therefore, a person of ordinary skill in the art would have been motivated to apply a bias to character strings (nucleic acids), as stated by Selifonov et al., to a gene predicting program, as stated by Borodovsky et al., in order to make methods faster and more efficient for discovering new genes (Borodovsky et al., page 123, col. 1, paragraph 1).



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Thus, Borodovsky et al., in view of Selifonov et al., motivate claims 1, 4, 5, 7, 8, 9, 12, 13, 15, and 41-44.

### ***Conclusion***

No claim is allowed.

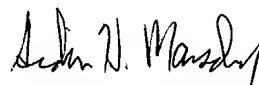
Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR §1.6(d)). The CM1 Fax Center number is (703) 872-9306.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carolyn Smith, whose telephone number is (703) 308-6043. The examiner can normally be reached Monday through Thursday from 8 A.M. to 6:30 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, can be reached on (703) 308-4028.

Any inquiry of a general nature or relating to the status of this application should be directed to Legal Instruments Examiner Tina Plunkett whose telephone number is (703) 305-3524 or to the Technical Center receptionist whose telephone number is (703) 308-0196.

December 8, 2003

  
ARDIN H. MARSCHEL  
PRIMARY EXAMINER